

CATGAAGGTTCCCTCCTGCTCCTGCTTCTCTTTCTTCTGCTCAGTGCGAGCTACTGAGCAACCGCAGGTGCTCACTG
 AGCATCCCAGCATGAGGCGAGCCCTGACCGGGGCCAAGGCTCCTCGCACTTCTGGGCCAACTAAGCTTTCTCTGAC
 TGGCAGAACTTCGTGGGCGAGGAGACGTTATGGGGCCGAGTCCCAGAAACCCACGGTGAAAGCACTGCTCATCGTGCC
 CTACTCATTACCATCGCTTCTCTGCTCTTCTGGTAATGTCCTGGTCTGTCATGTCATCTTCAAGAACCAGCGCATGC
 ACTCGGCCACCGAGCCTCTTCAATTGTCACCTGGCAGTGGCGGACATCATGATCACATTGCTCAACACGCGCTTCACT
 TTGGTCCGCTTTGTGAACAGCACATGGGTGTTTGGGAAGGGCATGTCATGTCAGTCGCTTTGCTCAGTACTGTTT
 TCTACATGCTCTCAGCACTGACTCTGACAGCTATCGCAGTGGACCGCCACCGAGTTCATCATGCATCCACTGAAGCCTC
 GGATCTCCATCACCAAGGGTGTCATATATATTGCTGTCATCTGGGTTCATGGCTACCTTCTTCTCTCTGCCACATGCC
 ATCTGCCAGAACTGTTTACCCTTCAAGTACAGTGAGGACATTGTCGCGCTCCCTCTGCTTGGCGGACTTCCCGGAGCC
 AGCTGACCTCTTCTGGAAGTATCTGGACCTGGCCACCTTTCATCCTGCTCTACCTACTTCCACTCTTTCATTATCTCAG
 TGGCCATATGCTGCTGCTGGCCAAAGAAGCTGTGGCTCTGTAAACACCATTTGGCGAGCTGACCACAGAGCAGTACCTCGCC
 CTGGGAGCGCAAGAAGAAGAACCCGTGAAGATGCTGGTGGCTGTGGTAGTCTCTTTGGCCCTCTGCTGGTTCCTCTCT
 CAACTGCTATGTCCTCCTCTCTGTCAGCAAGGCCATCCAGACCAACAATGCCCCCTACTTTGCTTCCACTGCTTTT
 CCATGAGCAGTACTTGTATATAACCCCTTCATCTACTGCTGGCTCAATGAGAAGCTTTAGGGCTGAGCTTAAGGCATTG
 CTGAGCATGTGCCAAAGGCCACCCAAAGCCGCGAGGAAGACAGGCTACCTTCCCCAGTTCCTTCTTCCAGGGTGGCATG
 GACAGAGAAGAGCCATGGTGGGAGGGCTCCACTACCTAATCACCACTTTGCCCTCTTCCCCAGATCCAGTCTGGGAAGA
 CAGATCTGTCATCTGTGGAACCCGTTGTGGCCATGAGTTAGGGAAAGCTGGAAGTTGGTGGGGGAGGGTTCTTTCTCT
 CTCACAATTGACCAGACACTAACAGAGTGTGGAAGTAACACAGAGCAGTGAGATGCTTTGGGTTCCTAGGAACCTGT
 CCAGCCCCATCTGATTTGCAAACTTTCTAGAAGATGCCATGAGGTGGTGTGTGTAGATCTTTGAGCAAGAGCTCTGG
 AAACCACCTCAGCTTCAACAGAGGCTGGTCCAGTCAACCACCTCCAATTGTGTAGCATCTGCCACCTTGGCCCTTCTCT
 ACTGCTTGAGCAACCACAGGGGGACTTGAGCCATACTATTGGTGGGCTTGGCCCCACATGCTCAGAAAAGAACAGGCAC
 AAAGGCTTTCTGAAGTCATTGGAACAGGAATAATCACACAGCTTCAGTGACCTTGGCTCTATCCATGACCAGACAGG
 ACCCATTTTGGCTTCTTAAAAACAAAGAGAAATTAGTATTGCCACTTTGAAAAGTTTCAAGAAAAGTAAAGAAATGAGT
 TCAGCCCTCAATTTGTAAGAAAAGGAAAAAGAAAAAGAAAAAGAAAAAGAAAAAGAAAAAGCCTGTTAATATGCTGTA
 AATTTATCTGTAGCTTTGGCTTCTGTGTGTGTACATTTGTACTTTTAAAAATCCTGAACTACACGTGTCCATGTAGAT
 TGTAAATAATTAGCAAGAACTGGAAATATATCAGAGTATTATTGAATTC (SEQ ID NO:1)

MKVPPVLLLFLLSSVRATEQPQVVTEHPSMEAALTGPNASSHFWANYTFSDWQNFVGRRRYGAESQNPTVKALLIVA
 YSFTIVFSLFGNVLVCHVIFKNQRMHSATSLFIVNLAVADIMITLLNTPFTLVRFVNSTWVFGKGMCHVSRFAQYCS
 LHVSAITLTAIAVDRHQVIMHPLKPRISITKGVIYIAVIW/MATFFSLPHAICQKLFTFKYSEDIVRSLCLPDPFPEP
 ADLFWKYLDLATFILLYLLPLFIISVAYARVAKKLWLCNTIGDVTTEQYLALRRKKKTTVKMLVLVVVLFALCWFLPL
 NCYVLLLSKAIHTNNALYFAFWFAMSSTCYNPFICYWLNENFRVELKALLSMCQRPPKPKQEDRLPSPVPSFRVAW
 TEKSHGRRAPLPNHHLPSQIQSGKTDLSSVEPVVAMS (SEQ ID NO:2)

FIGURE 1

Underlined = deleted in targeting construct

Bold = sequence flanking Neo insert in targeting construct

GGGGTGGCAGTCGGCACCATCAGGCTCCCTTGGCGTTTCGGAGTTTTCTCTGTGGTCCCG
 ACTCTCCGGAGGATCTCGGTTGTCTCCCAAGTCGGAACCTGGCACGGTCCAGGTTCACTC
 GGAGGTCGGGGCTTCCTCTGTGCCCCGTGCCCTCGCTCCCAGGCTCCCTCTGTGGTGTG
 GACTCCTCTAGCCCGGTGCGCTCAGCCCCCTCGCACCCAGCCTCCAGGCACAGAGCCCGGC
 AGGGAGCTCAGCCCTTGTGCCTAGAGCTGCAGTGGCTGGACATGAAGGTTCTCCTGTCC
 TGCTTCTCTTTCTCTGTCTCAGTGCGAGCTACTGAGCAACCGCAGGTCTCACTGAGC
 ATCCAGCATGGAGGCAGCCCTGACCGGGCCCAACGCCTCCTCGCACTTCTGGGCAACT
 ACACITTTCTCTGACTGGCAGAACTTCTGGGTCAGGAGACGTTATGGGGCCGAGTCCCAGA
 ACCCCACCGGTGAAAGCACTGCTCATCGTGGGCTACTCATTCACCATGCTCTTCTCGCTCT
 TCGGTAATGTCTGGTCTGTCTATCTTCAAGAACCAGCCCATGCACTCGGGCCACCA
 GCCTCTTCAATTGTCAACCTGGCAGTGGCGGACATCATGATCAGATTGCTCAACACGCCCT
 TCACTTTGGTCCGCTTTTGTGAACAGCACATGGGTGTTTGGGAAGGGCATGTGTATGTCA
 GTGCGCTTTGCTCAGTACTGTTCTCTACATGTCT**CAGCACTGACTCTGACAGCTATCGCAG**
TGGACCGCCACCAGTCAATCATGCATCCACTGAAGCCTCGGATCTCCATCACCAGGGTG
 TCATATATATTGCTGTCTATCTGGGTCTATGGCTACCTTCTTCTCTCTGCCACATGCCATCT
 GCCAGAACTGTCTTACCTTCAAGTACAGTGAAGGACATTGTGCGCTCCCTCTGCGTGGCGG
 ACTTCCCGGAGCCAGCTGACCTCTTCTGGAAGTATCTGGACCTGGCCACCTTCATCCTGC
 TCTACCTACTTCCACTCTTCAATATCTCAGTGGGCTATGCTCGTGTGGCCAAAGAAGCTGT
 GGCCTCTGTAAACACCATTTGGCGAGCTGACCACAGAGCAGTACCTCGCCCTGGCGACGCAAGA
 AGAAGACCACCGTGAAAGATGCTGGTGTCTTGTGGTAGTCCCTCTTTGCCCTCTGCTGGTTCC
 CTCFCAACTGCTATGTCTCTCTTGTCCAGCAAGGCCATCCACACCAACAATGCCCTCT
 ACTTTGCCCTTCCACTGGTTTGGCATGAGCAGTACTTGTATAACCCCTTCATCTACTGCT
 GGCTCAATGAGAACTTTAGGGTTGAGCTTAAGGCATTGCTGAGCATGTGCCAAAGGCCAC
 CCAAGCCGCGAGGAAGACAGGCTACCCCTCCCGAGTTCCCTTCCCTCAGGGTGGCATGGACAG
 AGAAGAGCCATGGTGGGAGGGCTCCACTACCTAATCAACCACTTSCCTCTTCCAGATCC
 AGTCTGGGAAAGACAGATCTGTCTATCTGTGGAACCCGTTGTGGCCATGAGTTAGGGAAAGC
 TGGAAGTTGTGGGGGAGGCTTCTTCTCTCACAATTGACCAGACACTAACAGAGTTGG
 AAAGTAACACAGAAAGCAGTGAGATGCTTGGGTTCCTAGGAACCTGTCCAGCCCCATCTGA
 TTTGCAAACTTTCTAGAAGATGCCATGAGGTGGTGTGTGTAGATCTTTGAGCAAGAGCTC
 TGGAAACCACTCAGCTTCAACAGAGGCTGGTCCAGTCAACCACCTCCAATTGTGTAGCA
 TCTGCCACCTTGGCTTCCCTACTGCTGAGCAACCCACAGGGGGACTTGAGCCATACTATTG
 GTGGGCTTGGCCACATGCTCAGAAAAGAACAGGCACAAAGGCTTTCTGAAGTCATTGGA
 ACAGGAATAATCACACAGCTTCAGTGACCTTGGCTCTATCCATGACCAGACAGGACCCAT
 TTTGGCTTCTTAAAAACAAAGAGAAATTAGTATTGCCACTTTGAAAAGTTTCAGAAAAGTA
 AAGAAATGAGTTTCAGCCCTCAATTTGTAAAAAAGGAAAAAAGAAAAAAGAAAAAAG
 AAAGAAAAAAGCCTGTAAATATGCTGTAAATTTATCTGTAGCTTTGCCTTCTGTGTGTGT
 ACATTTGTACTTTTAAAAATCCTGAACTACACGTGTCCATGTAGATTGTAATAATTAGCAA
 GAAACTGGAATATATCAGAGTATTATTGAATTC

FIGURE 2A

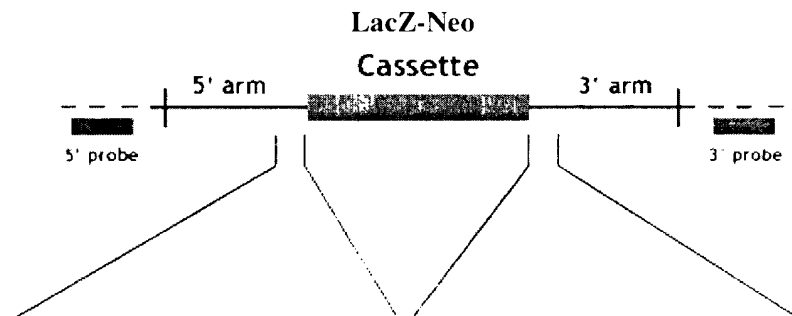
Gene Sequence Structure * 299 bp Sequence Deleted 753 bp

Size of partial
cDNA: 2253 bp



Targeting Vector*
(genomic sequence)
Construct Number: 463

Arm Length:
5': 2.5 kb
3': 0.6 kb



———— Targeting Vector
- - - - Endogenous Locus

* Not drawn to scale

5' > CTGGGCACGGTCCAGGTTCACT
CGGAGGCCCCGGGCTTCCTCTGTGC
CCCGTGCCCCCTCGCTCCCTGGCTC
CCTCTGTGGTGTGGACTCCTCTAG
CCCGGTGCGCTCAGCCCCCTCGCAC
CCAGCCTCCAGGCACAGAGCCCCGG
CAGGGAGCTCAGCCCTTGTGCCTA
GAGCTGCAGTGGCTGGACATGAAG
GTTTCTCCTGT < 3'
(SEQ ID NO:3)

5' > CAGCACTGACTCTGACAGCTA
TCGCAGTGGACCGCCACCAGGTGA
GAGCACCTGTCCCCAGCAGCATGC
TCCCATCTCCGTCTATGCCTGGCT
GGCTGGTGGGAATACTGCCACCAC
GGTCTGTAGGGAATACTCTCAGGA
CAGTGACTCATTTCAGTCCCGCTGA
CAGCGTGTGTGCTTGCCCTCCTTGT
TGATCAATTTG < 3'
(SEQ ID NO:4)

FIGURE 2B